

PATENT COOPERATION TREATY

REC'D 19 DEC 2005
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From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To: CATHY KODROFF HOWSON AND HOWSON SRPING HOUSE CORPORATE CENTER P.O. BOX 457 SPRINGS HOUSE, PA 19477			Date of mailing <i>(day/month/year)</i> 16 DEC 2005		
Applicant's or agent's file reference UPN-Q335SPCT			FOR FURTHER ACTION See paragraph 2 below		
International application No. PCT/US05/01768	International filing date <i>(day/month/year)</i> 21 January 2005 (21.01.2005)	Priority date <i>(day/month/year)</i> 23 January 2004 (23.01.2004)			
International Patent Classification (IPC) or both national classification and IPC IPC(7): C07K 1/00, 14/00; C07H 21/02, 21/04; A61K 31/70 and US Cl.: 530/350, 827; 53; 23.1-23.5; 514/44					
Applicant THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA					

1. This opinion contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion |
| <input type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input checked="" type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Date of completion of this opinion 07 November 2005 (07.11.2005)	Authorized officer Suzanne M. Mayer, Ph.D. Telephone No. 571-272-1600
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Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US05/01768

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☒ a sequence listing
☐ table(s) related to the sequence listing

b. format of material

- ☒ on paper
☒ in electronic form

c. time of filing/furnishing

- ☒ contained in the international application as filed.
☒ filed together with the international application in electronic form.
☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
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International appl.
PCT/US05/01768

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 9-15

because:

☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require an international search (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 9-15 are so unclear that no meaningful opinion could be formed (*specify*):

The claims are dependent upon 'any of claims 1-8'. There is no claim 3 in the application thus no meaningful search of these claims can be made.

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☐ no international search report has been established for said claims Nos. _____

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13^{ter}.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International appl.
PCT/US05/01758

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>6</u>	YES
	Claims <u>1,2,4,5,7-8 and 15-16</u>	NO
Inventive step (IS)	Claims <u>6</u>	YES
	Claims <u>1,2,4,5,7-8 and 15-16</u>	NO
Industrial applicability (IA)	Claims <u>1,2,4-8 and 15-16</u>	YES
	Claims <u>1,2,4-8 and 15-16</u>	NO

2. Citations and explanations:

Claims 1,2,4,5, 7-8 and 16-17 lack novelty and inventive step under PCT Article 33(2) and 33(3) as being anticipated by TINSLEY et al. (US 6,518,413). Utrophin is a 3,433 amino acid protein with several different regions and domains and which is usually found in muscle tissues. Tinsley et al. teach a DNA molecule that is a utrophin "mini-gene" which expresses a polypeptide that encodes for a 2008 amino acid protein which possesses the N-terminal amino acid domain, and the C-terminal amino acid domain, but which is missing the majority of the central domain (approximately 1500 amino acids - attached amino acid sequence alignment of SEQ ID No: 5 and SEQ ID No: 8 of Tinsley et al.). The polynucleotide is clone is placed under the control of the human skeletal alpha-actin (HAS) promoter and regulatory regions (column 16, lines 55-62). This promoter is a muscle specific promoter. The DNA of the invention is used with adenovirus or retrovirus vectors (column 10, lines 1-3). Claim 2 is included in this rejection because the prior art suggests/teaches that utrophin only has two hinge regions. This is evidenced by van Deutekom et al. (Figure 1, p.776) and Winder et al.: "similarly utrophin is thought to contain 22 repeats and two hinges." (1st column, 1st line, p.28).

Claim 6 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest DNA that encodes a protein of SEQ ID Nos: 4, 2 and 5.

Claims 1-2, 4-8 and 16-17 meet the criteria set out in PCT Article 33(4), and thus possess industrial applicability because the subject matter claimed can be made or used in industry. The microtrophin DNA and encoded proteins described in this application would be useful in the medical industry as a potential treatment supplement for muscle wasting diseases such as muscular dystrophy.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US05/01758

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

The description is objected to as containing the following defect(s) under PCT Rule 66.2(a)(iii) in the form or contents thereof: The first page of the specification is missing.

The Brief Description of the Drawings section contains an error on p. 2, line 19. This line refers to Figures 3A-2K, it should refer to Figures 3A-3K.

Claims 1-17 are objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: There is no claim # 3 in the claim set. Thus the claims are incorrectly numbered after claim 2 and onwards.

WRITTEN OPINION OF THE
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International application No.

PCT/US05/01768

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 2-8 and 16-17 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 2-8 and 16-17 are indefinite for the following reason(s): The independent claim is drawn to a DNA molecule. However, the inconsistent use of DNA terminology and protein (e.g. amino acid) terminology renders the claims indefinite. For example, in claim 6, the recitation of a nucleic acid according to claim 1, where the microtrophin is selected from the group having the amino acid sequence of SEQ ID No: 4. Correct claim construction in this circumstance dictates that the nucleic acid must encode for a protein having an amino acid sequence.

Claim 6 is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claim 6 is indefinite for the following reason(s): Claim 6 recites a microtrophin selected from the group consisting of human, canine and mouse microtrophin having the amino acid sequences of SEQ ID Nos: 4, 2 and 5, respectively. However, "microtrophin" is not a naturally occurring protein. Instead the term is defined by Applicants themselves and it they are non-naturally occurring protein derived from human, canine and mouse, but not endogenous. Thus, claims a human microtrophin having the amino acid sequence of SEQ ID No: 4, for example, is wholly inaccurate and misleading.



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Date

04.05.06

Reference	Application No./Patent No. 05804740.8 - 2101
Applicant/Proprietor THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA	

The international search report, or the declaration under Article 17(2)(a) PCT, has been published under Article 21(3) and Rule 48 PCT on 27.04.06. That publication takes the place of the mention of publication of the European search report (Art. 157(1) EPC).

The request for examination must be filed within **six months** from the above date (Art. 94(2) in conjunction with Art. 157(1) EPC). It is not deemed to have been filed until the examination fee has been paid. However, under Article 22 or 39 PCT in conjunction with Article 150(2) and Rule 107(1) EPC, the time limit for filing it does not expire before the end of the 31st month from the filing date (or earliest priority date). Payment of the designation fees must also be made within the above-mentioned period (R. 107(1) EPC). The same applies also for the extension fees.

If the request for examination is not filed in due time, and at least one designation fee is not paid, the European patent application is deemed to be withdrawn (Art. 94(3), 79(3) and R. 108(1) EPC).

For more details see the Guide for applicants Part 2: PCT proceedings before the EPO-"Euro-PCT".

Receiving Section

